REMARKS

Claims 70 and 72-77 are pending in the application. Claims 70 and 73 are amended herein, without the addition of new matter. Claims 70 and 73-77 stand rejected on the grounds of alleged obviousness-type double patenting over claims 7-13 and 16-18 of U.S. Pat. No. 6,146,894. Claims 70 and 72-77 stand rejected on the grounds of alleged obviousness-type double patenting over claims 1, 3-7, and 12 of U.S. Pat. No. 6,808,894. Claims 70 and 72-77 stand rejected on the grounds of alleged obviousness-type double patenting over claims 1-3 and 6 of U.S. Pat. No. 6,825,038. Claims 70, and 72-77 stand rejected under 35 U.S.C. §112, second paragraph as allegedly indefinite. Claims 70 and 73 stand rejected under 35 U.S.C. §112, first paragraph for alleged failure to comply with the written description requirement. Claims 70, 72, 73, 76, and 77 stand rejected under 35 U.S.C. §112, first paragraph as allegedly not enabled. Claims 70, 73-75, and 77 stand rejected under 35 U.S.C. §102(b) as allegedly anticipated by Nicolaides *et al.* (1998) Mol. Cell. Biol. 18:1635-41 ("Nicolaides reference"). Claims 70 and 73-77 stand rejected under 35 U.S.C. §102(e) as allegedly anticipated by 6,146,894. Claims 70, and 72-77 stand rejected under 35 U.S.C. §103(a) as allegedly obvious over the Nicolaides reference in view of U.S. Pat. No. 6,825,038. Claims 70 and 73-77 stand rejected under 35 U.S.C. §103(a) as allegedly obvious over U.S. Pat. No. 6,146,894 in view of U.S. Pat. No. 6,825,038.

Double Patenting Rejections

The office action alleges that the present claims are obvious variants of the claims in the cited patents. Applicants disagree with the rejection. The claims as amended herein are not taught or suggested by the cited patent. More specifically, none of the cited patents teach or suggest the step of selecting cells comprising mutations in the gene of interest that enhance the antigenicity or immunogenicity of the protein encoded by the gene. Thus, the claims are patentably distinct from the cited patents.

Indefiniteness

The office action alleges that claim 70 does not provide a link between the selection and protein expression steps. Applicants disagree with the rejection because the claim is

clear on its face. Once a cell comprising a mutation in a gene of interest is selected, the gene can be expressed in any genetically stable cell appropriate in the art. By way of example, but not of limitation, the skilled artisan can stabilize the cell comprising the mutation and express the gene, or can isolate the mutated gene and express it in another cell that is genetically stable. Other cells and techniques for immunogen expression will be apparent to those of skill in the art. The particular expression system chosen is not critical. Because the claim inherently contains the link between the selection and expression steps, the claim is definite, and withdrawal of the rejection is warranted.

Written Description

The office action alleges that claims drawn to a truncated mutant of PMS2 encompass a large genus that is not sufficiently described by the specification and the claims. To the extent that the rejection is maintained against the currently amended claims, Applicants disagree.

To satisfy the written description requirement, a patent specification must describe the claimed invention in sufficient detail that one skilled in the art can reasonably conclude that the inventor had possession of the claimed invention. *See Vas-Cath, Inc. v. Mahurkar*, 935 F.2d 1555, 1563, 19 USPQ2d 1111, 1116 (Fed. Cir. 1991). An applicant shows possession of the claimed invention by describing the claimed invention with all of its limitations using such descriptive means as words, structures, figures, diagrams, and formulas that fully set forth the claimed invention. *Lockwood v. American Airlines, Inc.*, 107 F.3d 1565, 1572, 41 USPQ2d 1961, 1966 (Fed. Cir. 1997). Possession may be demonstrated by description of an actual reduction to practice, by showing that the invention was "ready for patenting" such as by the disclosure of drawings or structural chemical formulas that show that the invention was complete, or by describing distinguishing identifying characteristics sufficient to show that the applicant was in possession of the claimed invention, i.e., complete or partial structure, other physical and/or chemical properties, functional characteristics when coupled with a known or disclosed correlation between function and structure, or some combination of such characteristics. *See, e.g., Pfaff v. Wells Elecs., Inc.*, 525 U.S. 55, 68, 119 S. Ct. 304, 312, 48 USPQ2d 1641, 1647 (1998); *Enzo Biochem, Inc. v. Gen-Probe, Inc.*, 323 F.3d 956, 964, 63 USPQ2d 1609, 1613 (Fed. Cir. 2002).

The claims as amended recite polynucleotides comprising a dominant negative allele of PMS2. Applicants point out that the claims are directed to methods comprising PMS2 having a dominant negative function. Several species of PMS2 that exhibit the dominant negative function, including PMS2 and PMS2-134, of divergent species such as human and mouse that can be employed in the claimed methods have been disclosed by the specification, and these species constitute a substantial portion of any genus that might be alleged as covered by the claimed method. Those of skill in the art are capable of identifying PMS2 genes (structure), and are capable of identifying PMS2 genes that exhibit a dominant negative function (function) in a cell. The specification conveys to one of skill in the art that Applicants had possession of the claimed subject matter. Thus, the claimed subject matter is adequately described. Reconsideration and withdrawal of the rejection is requested.

The Federal Circuit in *Vas-Cath, Inc. v. Mahurkar* cited a Supreme Court opinion in stating that one purpose of section 112 was:

> to put the public in possession of what the party claims as his own invention, so as to ascertain if he claims anything that is in common use, or is already known, and to guard against prejudice or injury from the use of an invention which the party may otherwise innocently suppose not to be patented. It is, therefore, for the purpose of warning an innocent purchaser, or other person using a machine, of his infringement of the patent; and at the same time, of taking from the inventor the means of practising upon the credulity or the fears of other persons, by pretending that his invention is more than what it really is, or different from its ostensible objects, that the patentee is required to distinguish his invention in his specification.

935 F.2d 1555, 1561, 19 U.S.P.Q.2d 1111, 1117 (Fed. Cir. 1991) (citing *Evans v. Eaton*, 20 U.S. (7 Wheat.) 356 (1822)). Applicants' specification makes clear what the invention is so as to put the public on notice. There can be no dispute that Applicants have described what they now claim. The specification and originally filed claims provide literal support for the presently rejected claims, and, as discussed above, Applicants have set forth adequate structural and functional limitations in the claims to establish compliance with the written description requirement of section 112. Withdrawal of the rejection is thus respectfully requested.

Enablement

The office action alleges that the specification does not reasonably provide enablement for making the inventive cells using any truncation mutant of any PMS2. To the extent that the rejection is maintained against the currently amended claims, Applicants disagree.

An inventor need not enable every mode of making and using the invention, and the enablement requirement is fulfilled if any mode of making and using the invention is described. *Engel Industr. v. Lochformer Co.*, 946 F.2d 1528, 1533 (Fed. Cir. 1991) ("[t]he enablement requirement is met if the description enables **any** mode of making and using the invention")(emphasis added); see also *Invitrogen Corp. v. Clontech Labs., Inc.,* 429 F.3d 1052, 1071 (Fed. Cir. 2005) ("Enablement does not require the inventor to foresee every means of implementing an invention at pains of losing his patent franchise. Were it otherwise, claimed inventions would not include improved modes of practicing those inventions. Such narrow patent rights would rapidly become worthless as new modes of practicing the invention developed, and the inventor would lose the benefit of the patent bargain.")

Applicants have amended the claims to be directed to methods involving cells that express a gene encoding a preselected immunogen *in vitro*, which comprise introducing into such cells a polynucleotide comprising a dominant negative allele of PMS2. Multiple sequences of dominant negative alleles of PMS2, including PMS2 and PMS2-134 of widely divergent species, such as human and mouse, are disclosed in the specification. It was known in the art at the time of filing that full-length PMS2 as well as PMS2-134 can exert a dominant negative effect (see, *e.g.*, US Pat. No. 6,808,894). In addition, the specification provides detailed guidance for assessing defective mismatch repair (see, *e.g.,* Example 1). Applicants submit that multiple modes to practice the claimed invention have thus been provided.

In making a determination of enablement, the inquiry is not whether experimentation is required, but rather whether the experimentation required is *undue*. According to the Federal Circuit, "a considerable amount of experimentation is permissible, if it is merely routine, or if the specification in question provides a reasonable amount of guidance with respect to the direction in which the experimentation should proceed . . . ." *In re Wands,* 858 F.2d 731, 737 (Fed. Cir. 1988) (citations omitted).

It is within the skill in the art to assay for evidence of defects in MMR activity in a given cell, for example, to assay for mutations in an immunogen-encoding gene. Many assays are available to the skilled artisan for this purpose, and they are routinely practiced (see, *e.g.*, Examples 3 and 4). Furthermore, it is not undue experimentation to identify PMS2 genes, and screen candidate dominant negative alleles of the PMS2 genes to determine if the candidates exhibit a dominant negative phenotype. It is within the skill in the art to determine which candidates exhibit and do not exhibit the structural and functional features of dominant negative alleles of PMS2 described in the specification and known in the art. All of this can be accomplished using routine experimentation. Because various structural and functional features of dominant negative alleles of a MMR gene are described by the specification and are otherwise known in the art, the specification clearly sets forth the novel aspects of the invention and provides specific starting materials and the conditions under which the claims can be practiced, and this is all that the law requires.

In view of the substantial guidance and working examples provided by the specification and the level of skill in the art, one skilled in the art would have been able to substitute other polynucleotides comprising dominant negative alleles of PMS2 for those presently exemplified by Applicants according to the guiding principles of the instant specification with no more than routine experimentation. Reconsideration and withdrawal of the rejection is requested.

Rejections Under 35 U.S.C. §102

The office action alleges that the Nicolaides reference (102(b)), and U.S. Pat. No. 6,146,894 (102(e)) provide the limitations of the claimed invention. Applicants disagree. The cited art does not teach or suggest the step of selecting cells comprising mutations in the gene of interest that enhance the antigenicity or immunogenicity of the protein encoded by the gene. Because all of the limitations of the invention are not taught or suggested by either of the cited references, the claims are not anticipated. Accordingly, reconsideration and withdrawal of the rejection is requested.

Rejections Under 35 U.S.C. §103

The office action alleges that the Nicolaides reference or U.S. Pat. No. 6,146,894 in combination with U.S. Pat. No. 6,825,038 render the claimed invention obvious. Applicants disagree. As described above, neither the Nicolaides reference nor the 6,146,894 patent provide the limitations of the claimed invention. The '038 patent does not remedy the deficiencies of the Nicolaides reference or the '894 patent because the '038 patent does not teach or suggest the step of selecting cells comprising mutations in the gene of interest that enhance the antigenicity or immunogenicity of the protein encoded by the gene. Because all of the limitations of the invention are not taught or suggested by the cited art, alone or in combination, a *prima facie* case for obviousness has not been established. Accordingly, reconsideration and withdrawal of the rejection is requested.

In view of the amendments submitted herewith and the foregoing remarks, Applicants respectfully assert that all claims presently pending are in condition for allowance. Favorable reconsideration and a Notice of Allowance are earnestly requested.

Respectfully submitted,

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